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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/875,520	06/06/2001	Phillip R. Hawkins	PF-0059-5 CON	6922

27904 7590 03/24/2004

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EXAMINER	
MURPHY, JOSEPH F	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/875,520	HAWKINS ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,24 and 28-44* is/are pending in the application.

4a) Of the above claim(s) *1,2,24,29,32,34,43 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28, 30-31, 33, 35-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 1-2, 24, 28-44 are pending. Claims 1-2, 24, 29, 32, 34, 43-44 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 28, 30-31, 33, 35-42 are under consideration.

Response to Amendment

The rejection of claims 28, 31, 33, 35-42 under 35 U.S.C. 102(b) as being anticipated by Baylink et al (WO 93/15107) has been obviated by Applicant's amendment and is thus withdrawn.

The rejection of claims 28, 30-31, 33, 35-42 under 35 U.S.C. 103(a) as being unpatentable over Baylink et al. (WO 93/15107) in view of U.S. Patent No. 5,530,101 (Queen et al.) has been obviated by Applicant's amendment and is thus withdrawn.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28, 30-31, 33, 35-42 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody which binds SEQ ID NO: 2, does not reasonably provide enablement for an antibody which binds a naturally-occurring amino acid sequence which is 90% identical to SEQ ID NO: 2, or comprising a biologically active fragment or immunogenic fragment of SEQ ID NO: 2, for reasons of record set forth in the Office Action of 10/02/2003. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 28, 30-31, 33, 35-42 are overly broad since insufficient guidance is provided as to which of the myriad of variant antigenic polypeptides encompassed by the claims which will retain the characteristics of the GIPL polypeptide. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of GIPL. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

Since the claims encompass antibodies which bind variant polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The claims as written do not set forth a functional limitation for the polypeptides encompassed by the claims to which the antibodies are directed. Since the amino acid sequence of a polypeptide determines its structural and functional

properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims.

Applicant argues that the recited variants are sufficiently similar to SEQ ID NO: 2 so as to retain the same structure to which the specific antibodies bind. However, Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass antibodies to polypeptides which the specification only teaches one skilled in the art to test for the ability to make antibodies specific fro SEQ ID NO: 2. It would require undue experimentation for one of skill in the art to make and use the claimed antibodies, since the skilled artisan would have to first make polypeptide variants of SEQ ID NO: 2, or immunogenic fragments thereof, then test for the ability to produce antibodies specific for SEQ ID NO: 2. Thus, since Applicant has only taught how to test for polypeptide variants of SEQ ID NO: 2 which produce antibodies specific for SEQ ID NO: 2, and has not taught how to make polypeptide variants of SEQ ID NO: 2, which produce antibodies specific for SEQ ID NO: 2, it would require undue experimentation of one of skill in the art to make and use the claimed antibodies.

Claims 28, 30-31, 33, 35-42 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in the Office Action of 10/02/2003. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The rejection of record set forth that these are genus claims. The claims are drawn to antibodies that bind naturally-occurring amino acid sequence having 90% identity to SEQ ID NO: 2, or an antibody which binds to an immunogenic fragment of SEQ ID NO: 2. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the encoded SEQ ID NO: 2. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the polypeptide of SEQ ID NO: 2 is insufficient

to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Applicant argues that the structural feature of the target polypeptide is that they are an immunogenic fragment of SEQ ID NO: 2, and that since binding determines antibody binding, one of skill in the art would not have difficulty in recognizing fragments of SEQ ID NO: 2. The claims are also drawn to antibodies which bind to sequence 90% identical to SEQ ID NO: 2. However, the instant disclosure of antibodies to SEQ ID NO: 2, does not adequately support the scope of the claimed genus. The issue here is similar to that considered by the court in Enzo Biochem v. Gen-Probe, Inc., 323 F.3d 956, 964 (Fed. Cir. 2002) ("Enzo Biochem II"), stated that "the written description requirement would be met for all of the claims [of the patent at issue] if the functional characteristic of [the claimed invention was] coupled with a disclosed correlation between that function and a structure that is sufficiently known or disclosed." Also, the court held that one might comply with the written description requirement by depositing the biological material with a public depository such as the American Type Culture Collection ("ATCC"). (Id. at 970). The court proffered an example of an invention successfully described by its functional characteristics. The court stated:

> For example, the PTO would find compliance with 112, paragraph 1, for a claim to an isolated antibody capable of binding to antigen X, notwithstanding the functional definition of the antibody, in light of the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature. (Id.) The court adopted the USPTO Guidelines as persuasive authority for the proposition that a claim directed to "any antibody which is capable of binding to antigen X" would have sufficient support in a written description that disclosed "fully characterized antigens."

Synopsis of Application of Written Description Guidelines, at 60, available at http://www.uspto.gov/web/menu/written.pdf (last visited Jan. 16, 2003). Therefore, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen. In the instant case, the specification does not provide sufficient support for the claims to the antibody that binds an immunogenic fragment, or which binds a naturally occurring variant 90% identical to SEQ ID NO: 2, because the Specification fails to disclose the structural elements of antibody or antigen. Applicant argues that the structural feature of the target polypeptide is that they are an immunogenic fragment of SEQ ID NO: 2, and that since binding determines antibody binding, one of skill in the art would not have difficulty in recognizing fragments of SEQ ID NO: 2. This argument fails, however, because Applicant did not sufficiently describe the antigen. If Applicant had sufficiently described the antigen, then the antibody could be claimed by simply stating its binding affinity for the "fully characterized" antigen. However, Applicant did not describe the antigen. Therefore, Applicant has attempted to define an unknown by its binding affinity to another unknown. As a result, the claims to the antibody which bind antibodies which bind to an immunogenic fragment of SEQ ID NO: 2 or bind to naturally occurring sequences 90% identical to SEQ ID NO: 2 lack written description.

Conclusion

Claims 28, 30-31, 33, 35-42 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The

examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
March 19, 2004

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